Epidemiology of nosocomial bloodstream infections in Estonia

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Summary A prospective multicentre hospital-wide surveillance study was performed to investigate nosocomial bloodstream infections (BSIs) and to promote BSI surveillance in Estonia in 2004–2005. All patients from the acute care departments of two referral centres and one central hospital were included. A total of 549 episodes of BSI occurred in 507 patients (0.6 cases per 1000 patient-days). Of those, 55% occurred in intensive care units and 47% were catheter-associated infections. Of BSI cases, 24% occurred in patients with haematological malignancy. The in-hospital case-fatality rate was 31%. Of causative micro-organisms, 315 (53%) were Gram-positive aerobes, 232 (39%) were Gram-negative aerobes and 35 (6%) were fungi. Anaerobic bacteria accounted for 2%. The most common pathogens were coagulase-negative staphylococci (26%), Enterobacteriaceae (24%), enterococci (13%) and pseudomonas (10%). Eight percent of BSI were polymicrobial. Seven percent of Staphylococcus aureus isolates were meticillin resistant. Of pseudomonas isolates, 19%, 25%, 30% and 44% were resistant to ceftazidime, meropenem, piperacillin/tazobactam and imipenem, respectively. The incidence of BSI did not differ significantly from other reported studies. With the exception of relatively high antimicrobial resistance among pseudomonas, the overall resistance patterns of Estonian nosocomial bloodstream pathogens were similar to those seen in Nordic countries and lower than in Central and Southern Europe.

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Introduction

Understanding the origins, treatment and outcomes of nosocomial bloodstream infections (BSIs) is important because these are among the most frequent and severe infectious complications of hospitalisation and medical care. BSIs are the cornerstone of prevention and control since they facilitate the development of appropriate intervention measures and help to evaluate their efficacy.

Several national and international networks for the surveillance of healthcare-associated infections have been established in Europe, but no hospital-wide multicentre surveillance of BSI from East-Central European countries has been published. Before 2004 there was no systematic surveillance of healthcare-associated infection in Estonia. This study was performed to assess the epidemiological features of BSI together with the species distribution and antimicrobial susceptibility of causative pathogens. Its secondary aim was to promote BSI surveillance at hospital level.

Methods

Hospitals and patients

Three Estonian hospitals participated: two referral centres, with 944 and 1236 beds, and one central hospital with 588 beds.

Data collection

In this prospective hospital-wide surveillance study, clinical and microbiological data were collected by local infection control personnel using a standardised case-report form. One investigator (P.M.) trained all infection control personnel and checked the completed forms for errors. Information routinely collected included age, sex, date of admission, date of the first positive blood culture, location of the patient at the onset of BSI (ward), isolated micro-organism(s) and antimicrobial susceptibility, probable source of bacteraemia/fungaemia and antimicrobial therapy on the day of sampling. The following predisposing clinical conditions were documented: intravascular catheter, indwelling urinary catheter, nasogastric tube, neutropenia, chemotherapy or surgery during the previous 30 days, organ transplantation, mechanical ventilation and total parenteral nutrition. Survival status was evaluated one week after the onset of BSI and at the end of the hospital stay.

Definitions

The CDC (Centers for Disease Control and Prevention, Atlanta, Georgia, USA) definition of BSI was used. Only laboratory-confirmed, nosocomial cases were included. If BSI occurred more than 48 h after admission, or resulted from earlier hospitalisation within previous 30 days, the episode was classified as nosocomial. Intensive care unit (ICU)-acquired BSI was defined as bacteraemia developing after 48 h of admission to ICU. BSI was classified as primary (vascular catheter-associated or of unknown origin) or secondary to infection at a distant body site. When an indistinguishable organism was isolated within seven days of previously documented BSI this was considered to belong to the same episode. Polymicrobial BSI was defined as the isolation of different species from one or more blood cultures within 48 h.

Treatment of BSI was considered to have been appropriate if, on the day of sampling, the patient was receiving at least one antimicrobial that was active in vitro against the implicated pathogen.

Microbiological methods

Blood cultures were processed using Bactec 9000 (Becton Dickinson, USA, two hospitals) and BacT/Alert 3D (bioMérieux, Marcy l’Etoile, France, one hospital). Antimicrobial susceptibility was determined in each centre by disc diffusion according to Clinical and Laboratory Standards Institute recommendation and/or E-tests (AB Biodisk, Solna, Sweden), used according to the manufacturer’s recommendation.

Statistical analysis

Descriptive analysis was performed using Stata 9.0 (Stata Corp., College Station, TX, USA). For...
significance associations χ²-test or Fisher’s two-tailed test was used.

Results

During the study period from January 2004 to December 2005, 549 episodes of BSI were recorded among 507 patients. The overall incidence of BSI across the three hospitals was 0.6 per 1000 patient-days (range: 0.2–0.8) and 3.1 per 1000 admissions (range: 0.7–4.3). The rate of sampling was 17 blood culture sets per 1000 patient-days (range: 13–21).

Study population and patient characteristics

The mean age of patients with BSI was 50 ± 25.5 years (range: <1–92 years). Forty-four episodes (8%) occurred in neonates (<28 days of age) and 46 (10%) in paediatric patients (≤16 years of age). Fifty-nine percent of patients were male.

Intravascular devices were the most common potential predisposing factor: central venous catheters were in place in 423 patients (77%), arterial catheters in 254 (46%) patients, and 280 patients (51%) had two or more intravascular catheters. Other potential predisposing factors were: urinary catheters in 279 patients (51%), mechanical ventilation in 222 (40%), nasogastric tube in 213 (39%), total parenteral nutrition in 132 (24%), neutropenia in 109 (20%), chemotherapy in 126 (23%) and surgery within the preceding 30 days in 220 (40%).

Episodes of BSI

Fifty-four percent of BSI episodes were reported in ICUs, 24% in haematology units, 11% in surgical units, 7% in internal medicine units and 4% in other units. The incidence of BSI per 1000 patient-days was 5.9 (range: 4.4–7.4) and 0.3 (range: 0.1–0.4) in ICU and non-ICU wards respectively.

Most (92%) BSI presented during the hospital stay in which it was acquired, 8% was related to previous hospitalisation. The median interval between admission and BSI was 13 days (range: 0–124). The median length of stay was 33 days (range: 1–213) in total, and 16 days (range: 0–208) following BSI.

Over half of episodes (321, 58%) were primary (257 vascular catheter-associated, 64 of unknown source) while 228 (42%) were secondary. Among secondary episodes the lower respiratory tract was the most common source (32% of all secondary cases). Catheter-related BSI and pneumonia were more frequent among BSI acquired in ICU (Table I). A total of 258 patients (47%) were receiving appropriate antimicrobial therapy on the day of sampling.

Overall, 157 of the patients with BSI died during hospitalisation, an in-hospital case-fatality rate of 31%. Among these, 60 (38%) died within one week of onset of BSI. The highest case-fatality rates occurred with intra-abdominal and surgical site sources (Table I).

Microbiological results

A total of 593 pathogenic micro-organisms were isolated. Of these, 315 (53%) were Gram positive, 232 (39%) were Gram-negative aerobes, 35 (6%) were fungi and 11 (2%) were anaerobes. Coagulase-negative staphylococci (CoNS), Enterobacteriaceae and enterococci were the most frequently isolated pathogens (Table II). BSI due to Pseudomonas spp., CoNS and Candida spp. was significantly more common among ICU than non-ICU cases. BSIs in non-ICU patients were significantly more

<table>
<thead>
<tr>
<th>Source</th>
<th>Total N = 549 (100%)</th>
<th>Non-ICU N = 253 (100%)</th>
<th>ICU N = 296 (100%)</th>
<th>P</th>
<th>In-hospital case fatality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary BSI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascular catheter-related</td>
<td>257 (47)</td>
<td>96 (37.9)</td>
<td>161 (54.4)</td>
<td>0.0001</td>
<td>31</td>
</tr>
<tr>
<td>Unknown</td>
<td>64 (12)</td>
<td>47 (18.6)</td>
<td>17 (5.7)</td>
<td>&lt;0.0001</td>
<td>23</td>
</tr>
<tr>
<td><strong>Secondary BSI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower respiratory tract</td>
<td>74 (13)</td>
<td>25 (9.9)</td>
<td>49 (16.6)</td>
<td>0.023</td>
<td>39</td>
</tr>
<tr>
<td>Skin/soft tissue</td>
<td>37 (7)</td>
<td>26 (10.3)</td>
<td>11 (3.7)</td>
<td>0.002</td>
<td>14</td>
</tr>
<tr>
<td>Surgical site</td>
<td>28 (5)</td>
<td>14 (5.5)</td>
<td>14 (4.7)</td>
<td>0.670</td>
<td>46</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>27 (5)</td>
<td>14 (5.5)</td>
<td>13 (4.5)</td>
<td>0.538</td>
<td>19</td>
</tr>
<tr>
<td>Intra-abdominal</td>
<td>26 (4)</td>
<td>9 (3.6)</td>
<td>17 (5.7)</td>
<td>0.229</td>
<td>54</td>
</tr>
<tr>
<td>Other</td>
<td>36 (7)</td>
<td>22 (8.7)</td>
<td>14 (4.7)</td>
<td>0.061</td>
<td>39</td>
</tr>
</tbody>
</table>

BSI, bloodstream infection; ICU, intensive care unit.

a Significantly (P < 0.05) more frequently detected as a source of BSI episodes of fatalities than in survivors.
often caused by *S. aureus* and *E. coli*. Among the 35 fungal isolates *C. albicans* was the most common (23 isolates, 66%). Among neutropenic patients the most frequent isolates were CoNS (28 of 113 isolates, 25%), *E. coli* (19 isolates, 17%) and enterococci (19 isolates, 17%). In-hospital case-fatality ranged from 15% for *S. aureus* to 57% for enterococci (Table II).

Antimicrobial susceptibility data are presented in Tables III and IV. One *E. coli* and three *Klebsiella* spp. produced extended-spectrum β-lactamase.

**Discussion**

Hospital-wide multicentre surveillance data on BSI in Europe have been reported from England, Belgium and Finland, where the mean rates were 0.6, 0.7 and 0.8 per 1000 patient-days respectively.9–11 In the SCOPE Project from the USA the incidence of BSI was 6 cases per 1000 admissions.12 The overall incidence in this study (0.6 per 1000 patient days and 3.1 per 1000 admissions) does not differ significantly from other reported studies although the figures may not be strictly comparable because the mean number of blood culture sets in Estonia, 17 per 1000 patient days, is lower than that reported from most European countries.13

Intravascular devices were the most common sources of BSI in our study. It is possible that by using clinical and blood culture data we have overestimated the importance of vascular catheters because device colonisation was not always laboratory-confirmed. However, this approach corresponds more closely to clinical circumstances and may represent a better way to compare BSI rates in surveillance studies.14 According to our data, surveillance and efforts for prevention should be primarily targeted at central intravascular devices in high risk specialties such as ICU and haematology. It is possible that our finding that CoNS were the most frequent cause of BSI is overestimated due to contamination. The CDC definition of BSI has intermediate sensitivity and specificity for true BSI but this is the most commonly used definition and numerous studies have documented similar findings.11,12,15–18

**Table II** Most common causative pathogens in 549 episodes of nosocomial BSI stratified according to clinical setting (ICU vs non-ICU wards), and associated in-hospital case-fatality rates

<table>
<thead>
<tr>
<th>Micro-organism</th>
<th>Total N = 593 (100%)</th>
<th>Non-ICU N = 272 (100%)</th>
<th>ICU N = 321 (100%)</th>
<th>P</th>
<th>In-hospital case-fatality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CoNS</td>
<td>152 (26)</td>
<td>57 (21)</td>
<td>95 (30)</td>
<td>0.018</td>
<td>24</td>
</tr>
<tr>
<td>Enterococcus spp.</td>
<td>76 (13)</td>
<td>40 (15)</td>
<td>36 (11)</td>
<td>0.219</td>
<td>57&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Pseudomonas spp.</td>
<td>57 (10)</td>
<td>12 (4)</td>
<td>45 (14)</td>
<td>0.0001</td>
<td>44&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>54 (9)</td>
<td>35 (13)</td>
<td>19 (6)</td>
<td>0.004</td>
<td>15</td>
</tr>
<tr>
<td>Klebsiella spp.</td>
<td>52 (9)</td>
<td>24 (9)</td>
<td>28 (9)</td>
<td>1.0</td>
<td>21</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>49 (8)</td>
<td>35 (13)</td>
<td>14 (4)</td>
<td>0.0003</td>
<td>29</td>
</tr>
<tr>
<td>Other Enterobacteriaceae</td>
<td>44 (7)</td>
<td>18 (7)</td>
<td>26 (8)</td>
<td>0.53</td>
<td>39</td>
</tr>
<tr>
<td>Candida spp.</td>
<td>35 (6)</td>
<td>6 (2)</td>
<td>29 (9)</td>
<td>0.0004</td>
<td>51&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Acinetobacter spp.</td>
<td>20 (3)</td>
<td>5 (2)</td>
<td>15 (5)</td>
<td>0.07</td>
<td>25</td>
</tr>
</tbody>
</table>

BSI, bloodstream infection; ICU, intensive care unit; CoNS, coagulase-negative staphylococci.

<sup>a</sup> Significantly (P < 0.05) more frequently detected as pathogen of BSI episodes of fatalities than in survivors.

**Table III** Antimicrobial resistance among Gram-positive organisms most frequently isolated from patients with nosocomial bloodstream infection

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Percentage of resistant isolates (no. of resistant isolates/no. tested) among Gram-positive bacteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CoNS</td>
</tr>
<tr>
<td>Oxacillin</td>
<td>83 (126/152)</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>–</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>70 (95/135)</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>55 (65/119)</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>73 (88/121)</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>76 (106/140)</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>0 (0/152)</td>
</tr>
</tbody>
</table>

CoNS, coagulase-negative staphylococci.
In our study enterococcal BSI was very frequent. Enterococcal BSIs have become more common over the past two decades and according to the SCOPE project they represent the third most common cause of nosocomial BSI in the USA.\textsuperscript{12}

The most commonly isolated Gram-negative organisms in our series (Enterobacteriaceae and pseudomonas) have been among the leading Gram-negative pathogens in other studies.\textsuperscript{9} In our study the proportions of BSI caused by \textit{S. aureus} and \textit{Candida} spp. were lower than those reported elsewhere, as was the proportion of polymicrobial BSI.\textsuperscript{9–12}

Empirical treatment of patients with BSIs has become more complicated in an era of increasing antimicrobial resistance. According to our data, 53% of patients were receiving antibacterial therapy on the day of sampling that subsequently proved to be ineffective.

The rate of MRSA was higher than that identified in Nordic countries and The Netherlands but lower than rates reported from Central and Southern European countries.\textsuperscript{6,13} In the USA, data from hospitals participating in SCOPE showed that 41% of bloodstream \textit{S. aureus} strains were meticillin resistant.\textsuperscript{12} The prevalence of antibiotic resistance among \textit{Pseudomonas} spp. was higher in our study than that reported in the USA (SCOPE) and in European studies.\textsuperscript{9,11,12}

The case-fatality rate observed in our study (31%) is consistent with previous investigations.\textsuperscript{12,18} Mortality rates were highest for infections caused by enterococci (57%) and \textit{Candida} spp. (51%). In the SCOPE project, the crude in-hospital mortality rates varied with aetiology from 21% for CoNS to 39% for \textit{P. aeruginosa} and \textit{Candida} spp.\textsuperscript{12}

In this prospective hospital-wide multicentre study we recorded the occurrence, origin, severity and aetiology of BSI for the first time in Estonia. We believe that due to the involvement of the largest hospitals, the results provide a reliable assessment of the epidemiology of BSI in Estonia during the period. We hope that the study will contribute to the development and implementation of surveillance in Estonian hospitals.

\textbf{Acknowledgements}

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\textbf{Conflict of interest statement}

None declared.

\textbf{Funding source}

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\textbf{References}